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=> d que
L1            29 SEA FILE=CAPLUS LERCANIDIPINE(W)HYDROCHLORIDE
L2             3 SEA FILE=CAPLUS L1 AND CRYSTAL?


=> d l2 1-3 ibib abs hit

L2   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:194018  CAPLUS
DOCUMENT NUMBER:          144:260839
TITLE:                    Preparation of lercanidipine salts
INVENTOR(S):              Leonardi, Amadeo; Motta, Gianni; Von Raumer, Markus
PATENT ASSIGNEE(S):       Recordati Ireland Limited, Ire.; Recordati Industria
                          Chimica E Farmaceutica S.p.A.
SOURCE:                   PCT Int. Appl., 41 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2006021397         A1    20060302    WO 2005-EP9043          20050822
     WO 2006021397         C1    20060427
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     US 2006047125         A1    20060302    US 2005-211769          20050824
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PRIORITY APPLN. INFO.: US 2004-604149P P 20040824

AB The invention relates to new addition salts comprising lercanidipine and an acid counterion selected from the group consisting of: (i) inorg. acids, (ii) sulfonic acids, (iii) monocarboxylic acids, (iv) dicarboxylic acids, (v) tricarboxylic acids, and (vi) aromatic sulfonimides, with the proviso that said acid counterion is not hydrochloric acid. In particular, both amorphous and crystalline salts of lercanidipine with benzenesulfonic and naphthalene-1,5-disulfonic acids are disclosed, as are amorphous salts of lercanidipine with several other acid counterions. Thus, lercanidipine besylate was prepared and characterized by Raman spectroscopy.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Crystal structure
Polymorphism (crystal)
(of lercanidipine salts)

IT 100427-26-7DP, Lercanidipine, salts 132866-11-6P, Lercanidipine hydrochloride 877372-41-3P 877372-42-4P 877372-43-5P 877372-44-6P 877372-45-7P 877372-46-8P 877372-47-9P 877372-48-0P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lercanidipine salts)

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:133241 CAPLUS
DOCUMENT NUMBER: 138:175893
TITLE: Solvates and crystalline forms of lercanidipine hydrochloride
INVENTOR(S): Leonardi, Amedeo; De Iasi, Gianluca; Bonifacio, Fausto
PATENT ASSIGNEE(S): Recordati Ireland Limited, Ire.
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014085	A1	20030220	WO 2002-EP8700	20020805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1423367	A1	20040602	EP 2002-767318	20020805
EP 1423367	B1	20050427		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011738	A	20040928	BR 2002-11738	20020805
HU 200401161	A2	20040928	HU 2004-1161	20020805
CN 1538958	A	20041020	CN 2002-815511	20020805
JP 2005502648	T2	20050127	JP 2003-519035	20020805
AT 294162	E	20050515	AT 2002-767318	20020805
CA 2399459	AA	20030206	CA 2002-2399459	20020806
CA 2399583	AA	20030206	CA 2002-2399583	20020806
US 2003069285	A1	20030410	US 2002-214385	20020806
US 2003083355	A1	20030501	US 2002-214386	20020806
US 6852737	B2	20050208		

NO 2004000479	A	20040203	NO 2004-479		20040203
US 2004204459	A1	20041014	US 2004-782376		20040218
US 2005192323	A1	20050901	US 2005-48646		20050131
US 2005239847	A1	20051027	US 2005-48647		20050131
PRIORITY APPLN. INFO.:			IT 2001-MI1727	A.	20010806
			IT 2001-MI1726	A	20010806
			US 2002-367789P	P	20020326
			CA 2002-2380202	A	20020403
			WO 2002-EP8700	W	20020805
			US 2002-214386	A3	20020806

AB The invention describes new solvates of lercanidipine-HCl with organic solvents, new crystalline forms III and IV obtained from said solvates by removing solvation solvents, and pharmaceutical compns. containing as active agent at least one of the crystalline forms III and IV.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Solvates and crystalline forms of lercanidipine hydrochloride

ST lercanidipine hydrochloride solvate org cryst form

IT Crystal morphology
Crystallization
Drug delivery systems
Solvates
(solvates and crystalline forms of lercanidipine hydrochloride)

IT 75-09-2, Methylene chloride, reactions
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(solvates and crystalline forms of lercanidipine hydrochloride)

IT 132866-11-6P, Lercanidipine hydrochloride
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(solvates and crystalline forms of lercanidipine hydrochloride)

IT 497859-62-8P, Lercanidipine hydrochloride
497859-63-9P, Lercanidipine hydrochloride
497859-64-0P, Lercanidipine hydrochloride
497859-65-1P, Lercanidipine hydrochloride
497859-66-2P, Lercanidipine hydrochloride
497859-67-3P, Lercanidipine hydrochloride
497859-68-4P, Lercanidipine hydrochloride
497859-69-5P, Lercanidipine hydrochloride
497859-70-8P, Lercanidipine hydrochloride
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(solvates and crystalline forms of lercanidipine hydrochloride)

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2003:133240 CAPLUS
DOCUMENT NUMBER:	138:193269
TITLE:	Novel crystalline polymorphic forms of lercanidipine hydrochloride and process for their preparation
INVENTOR(S):	Bonifacio, Fausto; Campana, Francesco; De Iasi, Gianluca; Leonardi, Amedeo
PATENT ASSIGNEE(S):	Recordati Ireland Limited, Ire.
SOURCE:	PCT Int. Appl., 93 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014084	A1	20030220	WO 2002-EP8699	20020805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2380202	AA	20030206	CA 2002-2380202	20020403
EP 1432683	A1	20040630	EP 2002-762428	20020805
EP 1432683	B1	20051019		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011739	A	20040928	BR 2002-11739	20020805
HU 200401163	A2	20040928	HU 2004-1163	20020805
CN 1538957	A	20041020	CN 2002-815413	20020805
JP 2005504045	T2	20050210	JP 2003-519034	20020805
AT 307114	E	20051115	AT 2002-762428	20020805
IL 153917	A1	20051120	IL 2002-153917	20020805
EP 1600441	A2	20051130	EP 2005-106264	20020805
EP 1600441	A3	20051207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
NZ 531558	A	20051223	NZ 2002-531558	20020805
ES 2212759	T3	20060416	ES 2002-2762428	20020805
CA 2399459	AA	20030206	CA 2002-2399459	20020806
CA 2399583	AA	20030206	CA 2002-2399583	20020806
US 2003069285	A1	20030410	US 2002-214385	20020806
US 2003083355	A1	20030501	US 2002-214386	20020806
US 6852737	B2	20050208		
NO 2004000266	A	20040324	NO 2004-266	20040120
US 2004204459	A1	20041014	US 2004-782376	20040218
ZA 2004001806	A	20050418	ZA 2004-1806	20040304
HK 1067123	A1	20060526	HK 2004-110181	20041223
US 2005192323	A1	20050901	US 2005-48646	20050131
US 2005239847	A1	20051027	US 2005-48647	20050131

PRIORITY APPLN. INFO.:		
IT 2001-MI1726	A	20010806
US 2002-367789P	P	20020326
IT 2001-MI1727	A	20010806
CA 2002-2380202	A	20020403
EP 2002-762428	A3	20020805
WO 2002-EP8699	W	20020805
US 2002-214386	A3	20020806

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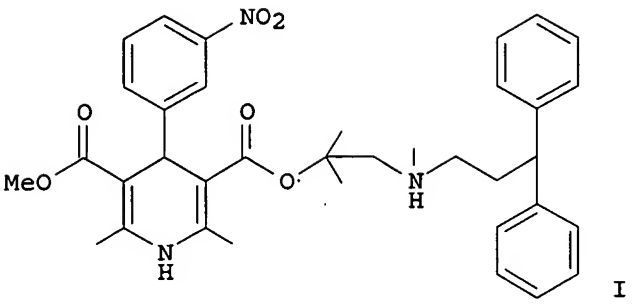


I

AB The invention describes novel lercanidipine (I) crude forms (A) and (B), novel I-HCl crystalline forms I and II obtained from crude forms, pharmaceutical, antihypertensive compns. containing as active agent at least one of the I-HCl crystalline forms I and II and methods of use. I-HCl was prepared and the crystalline forms obtained by crystallization from various solvents.

The bioavailability of the various forms was also determined

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Novel crystalline polymorphic forms of lercanidipine hydrochloride and process for their preparation

ST lercanidipine hydrochloride crystal form

IT Antihypertensives
Crystal morphology
Drug bioavailability
Human
(crystalline polymorphic forms of lercanidipine hydrochloride)

IT 132866-11-6P, Lercanidipine hydrochloride
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline polymorphic forms of lercanidipine hydrochloride)

IT 64-17-5, Ethanol, processes 67-63-0, Isopropanol, processes 141-78-6, Ethyl acetate, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(crystalline polymorphic forms of lercanidipine hydrochloride)

IT 74936-72-4 100442-33-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(crystalline polymorphic forms of lercanidipine hydrochloride)

IT 88712-56-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(crystalline polymorphic forms of lercanidipine hydrochloride)

=> d l1 1-29 ibib abs hit

L1 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:984461 CAPLUS
DOCUMENT NUMBER: 145:321533
TITLE: Solubilization method of lercanidipine hydrochloride and pharmaceutical preparation

manufactured therefrom for preventing degeneration of drug and increasing absorption of drug

INVENTOR(S): Chung, Yong Jin
PATENT ASSIGNEE(S): Human Pharm Co., Ltd., S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2006035422	A	20060426	KR 2004-84914	20041022

PRIORITY APPLN. INFO.: KR 2004-84914 20041022
AB A solubilization method of lercanidipine hydrochloride and a pharmaceutical preparation manufactured therefrom are provided to prevent degeneration of drugs, and increase absorption of drugs and improve the convenience and simplicity of handling of drugs. The lercanidipine hydrochloride is solubilized by mixing lercanidipine hydrochloride with at least one solubilizing agent selected from oleoyl macrogol-6 glycerides, polysorbate, linoleoyl macrogol-6-glycerides and diethylene glycol monoethyl ether in a weight ratio of 1:0.5-2.0 at 50-70°C. The pharmaceutical preparation of solubilized lercanidipine hydrochloride is prepared by mixing lercanidipine hydrochloride with at least one solubilizing agent selected from oleoyl macrogol-6 glycerides, polysorbate, linoleoyl macrogol-6-glycerides and diethylene glycol monoethyl ether in a weight ratio of 1:0.5-2.0, mixing the lercanidipine hydrochloride mixture with excipient, binding agent and disintegrant to prepare granules, and mixing the granules of lercanidipine hydrochloride with glidant.

TI Solubilization method of lercanidipine hydrochloride and pharmaceutical preparation manufactured therefrom for preventing degeneration of drug and increasing absorption of drug

AB A solubilization method of lercanidipine hydrochloride and a pharmaceutical preparation manufactured therefrom are provided to prevent degeneration of drugs, and increase absorption of drugs and improve the convenience and simplicity of handling of drugs. The lercanidipine hydrochloride is solubilized by mixing lercanidipine hydrochloride with at least one solubilizing agent selected from oleoyl macrogol-6 glycerides, polysorbate, linoleoyl macrogol-6-glycerides and diethylene glycol monoethyl ether in a weight ratio of 1:0.5-2.0 at 50-70°C. The pharmaceutical preparation of solubilized lercanidipine hydrochloride is prepared by mixing lercanidipine hydrochloride with at least one solubilizing agent selected from oleoyl macrogol-6 glycerides, polysorbate, linoleoyl macrogol-6-glycerides and diethylene glycol monoethyl ether in a weight ratio of 1:0.5-2.0, mixing the lercanidipine hydrochloride mixture with excipient, binding agent and disintegrant to prepare granules, and mixing the granules of lercanidipine hydrochloride with glidant.

IT Biological transport
(drug; solubilization method of lercanidipine hydrochloride)

IT Drug delivery systems
(granules; solubilization method of lercanidipine hydrochloride)

IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oleoyl macrogol-6, linoleoyl macrogol-6; solubilization method of lercanidipine hydrochloride)

IT Binders

Solubilization
Stability
(solubilization method of lercanidipine hydrochloride
)
IT Drug delivery systems
(tablet disintegrant; solubilization method of lercanidipine hydrochloride)
IT Biological transport
(uptake; solubilization method of lercanidipine hydrochloride)
IT 9005-63-4, Polyoxyethylene sorbitan
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polysorbates; solubilization method of lercanidipine hydrochloride)
IT 111-90-0, Diethylene glycol monoethyl ether 132866-11-6, Lercanidipine hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solubilization method of lercanidipine hydrochloride
)

L1 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:888104 CAPLUS
DOCUMENT NUMBER: 145:278324
TITLE: Lercanidipine free base
INVENTOR(S): Leonardi, Amedeo; Motta, Gianni; Berlati, Fabio; Candiani, Ilaria; Corcella, Francesco
PATENT ASSIGNEE(S): Recordati Ireland Limited, Ire.; Recordati Industria Chimica E Farmaceutica S.p.A.
SOURCE: PCT Int. Appl., 27pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006089788	A1	20060831	WO 2006-EP1783	20060224
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006199849	A1	20060907	US 2006-364861	20060227

PRIORITY APPLN. INFO.: US 2005-656741P P 20050225

AB The invention provides substantially pure lercanidipine free base, having a purity of at least 95 %, preferably at least about 97 %, more preferably at least about 99 %, and still more preferably at least about 99.5 %. The lercanidipine free base of the present invention is formed as an amorphous solid that is easily handled and particularly well suited to the formulation of pharmaceutical compns.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 100427-26-7P, Lercanidipine 132866-11-6P, Lercanidipine hydrochloride
RL: PEP (Physical, engineering or chemical process); PUR (Purification or

recovery); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(lercanidipine free base formulation)

L1 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:884456 CAPLUS
DOCUMENT NUMBER: 145:299398
TITLE: Amorphous lercanidipine hydrochloride
INVENTOR(S): Leonardi, Amedeo; Motta, Gianni; Berlati, Fabio
PATENT ASSIGNEE(S): Recordati Ireland Limited, Ire.; Recordati Industria Chimica E Farmaceutica S.p.A.
SOURCE: PCT Int. Appl., 30pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006089787	A1	20060831	WO 2006-EP1782	20060224
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006211742	A1	20060921	US 2006-364862	20060227

PRIORITY APPLN. INFO.: US 2005-656836P P 20050225

AB The invention provides a substantially pure amorphous lercanidipine-HCl having a purity of at least 95%, preferably at 99.5%. The invention further provides methods of preparing substantially pure amorphous lercanidipine, and pharmaceutical compns. containing the pure amorphous lercanidipine. An amorphous form of lercanidipine-HCl was prepared by dissolving the crystalline form in MeOH and heating the solution and precipitating it from a suspension formed.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Amorphous lercanidipine hydrochloride
ST lercanidipine hydrochloride amorphous form
IT Antioxidants
Binders
Dispersing agents
Dissolution
Drug bioavailability
Drug delivery systems
Dyes
Flavoring materials
Hydrophile-lipophile balance value
Lubricants
Particle size distribution
Pharmacokinetics
Plasticizers
Preservatives
Solubility

Sweetening agents
(amorphous lercanidipine hydrochloride)
IT Alcohols, uses
Amides, uses
Ketones, uses
RL: NUU (Other use, unclassified); USES (Uses)
(amorphous lercanidipine hydrochloride)
IT Edible oils
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous lercanidipine hydrochloride)
IT Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous lercanidipine hydrochloride)
IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous lercanidipine hydrochloride)
IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous lercanidipine hydrochloride)
IT Waxes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous lercanidipine hydrochloride)
IT Polar solvents
(aprotic; amorphous lercanidipine hydrochloride)
IT Drug delivery systems
(capsules, controlled-release; amorphous lercanidipine hydrochloride)
IT Hydrocarbons, uses
RL: NUU (Other use, unclassified); USES (Uses)
(chloro; amorphous lercanidipine hydrochloride)
IT Viscosity
(enhancers; amorphous lercanidipine hydrochloride)
IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters; amorphous lercanidipine hydrochloride)
IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyhydric, esters; amorphous lercanidipine hydrochloride)
IT Drug delivery systems
(tablets, coated; amorphous lercanidipine hydrochloride)
IT 64-17-5, Ethyl alcohol, uses 67-56-1, Methanol, uses 67-64-1, Acetone, uses 68-12-2, Dimethylformamide, uses 75-09-2, Methylene chloride, uses
RL: NUU (Other use, unclassified); USES (Uses)
(amorphous lercanidipine hydrochloride)
IT 132866-11-6, Lercanidipine hydrochloride
184866-29-3, (S)-Lercanidipine hydrochloride
187731-34-6, (R)-Lercanidipine hydrochloride
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous lercanidipine hydrochloride)
IT 9004-65-3, Hydroxypropyl methyl cellulose 9057-02-7, Pullulan 25322-68-3D, Polyethylene glycol, fatty acid esters 25322-69-4D, Polypropylene glycol, fatty acid esters
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous lercanidipine hydrochloride)

L1 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:853475 CAPLUS
DOCUMENT NUMBER: 145:471400
TITLE: Process for preparing lercanidipine

hydrochloride under mild condition with improved convenience and yield

INVENTOR(S): Choi, Jang Sik; Park, Chang Kwon; Suh, Jung Jin
PATENT ASSIGNEE(S): Kun Il Pharm. Co., Ltd., S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2005013348	A	20050204	KR 2003-51970	20030728

PRIORITY APPLN. INFO.: KR 2003-51970 20030728

AB A process for preparing lercanidipine hydrochloride [i.e., 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic acid 2-[(3,3-diphenylpropyl)methylamino]-1,1-dimethylethyl Me ester monohydrochloride] is provided, thereby producing lercanidipine hydrochloride on a large scale under mild condition with improved convenience and yield because a side-product is simply removed by using a coupling agent DCC. The process for preparing lercanidipine hydrochloride comprises the treatment of 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic acid monomethyl ester with 1-[(3,3-diphenylpropyl)methylamino]-2-methyl-2-propanol in the presence of a coupling agent and catalyst in solvent at 60-120°. The coupling agent is dicyclohexylcarbodiimide, 1-hydroxybenzotriazole or di-Et (cyano)phosphonate. The catalyst is 4-dimethylaminopyridine, N-hydroxysuccinimide, or 4-pyrrolidinopyridine. The solvent is toluene, xylene, DMF, chloroform, 1,2-dichloroethane or THF.

TI Process for preparing lercanidipine hydrochloride under mild condition with improved convenience and yield

AB A process for preparing lercanidipine hydrochloride [i.e., 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic acid 2-[(3,3-diphenylpropyl)methylamino]-1,1-dimethylethyl Me ester monohydrochloride] is provided, thereby producing lercanidipine hydrochloride on a large scale under mild condition with improved convenience and yield because a side-product is simply removed by using a coupling agent DCC. The process for preparing lercanidipine hydrochloride comprises the treatment of 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic acid monomethyl ester with 1-[(3,3-diphenylpropyl)methylamino]-2-methyl-2-propanol in the presence of a coupling agent and catalyst in solvent at 60-120°. The coupling agent is dicyclohexylcarbodiimide, 1-hydroxybenzotriazole or di-Et (cyano)phosphonate. The catalyst is 4-dimethylaminopyridine, N-hydroxysuccinimide, or 4-pyrrolidinopyridine. The solvent is toluene, xylene, DMF, chloroform, 1,2-dichloroethane or THF.

ST lercanidipine hydrochloride prepn

IT Coupling reaction
(preparation of lercanidipine hydrochloride via coupling reaction of dimethyl(nitrophenyl)pyridinedicarboxylic acid monomethyl ester with [(diphenylpropyl)methylamino](methyl)propanol)

IT 1122-58-3, 4-Dimethylaminopyridine 2456-81-7, 4-Pyrrolidinopyridine 6066-82-6, N-Hydroxysuccinimide
RL: CAT (Catalyst use); USES (Uses)
(preparation of lercanidipine hydrochloride via coupling reaction of dimethyl(nitrophenyl)pyridinedicarboxylic acid monomethyl ester with [(diphenylpropyl)methylamino](methyl)propanol)

IT 67-66-3, Chloroform, uses 68-12-2, Dimethylformamide, uses 107-06-2, 1,2-Dichloroethane, uses 108-88-3, Toluene, uses 1330-20-7, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of lercanidipine hydrochloride via coupling reaction of dimethyl(nitrophenyl)pyridinedicarboxylic acid monomethyl

ester with [(diphenylpropyl)methylamino](methyl)propanol)
IT 74936-72-4, (±)-1,4-Dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic acid monomethyl ester 100442-33-9, 1-[(3,3-Diphenylpropyl)methylamino]-2-methyl-2-propanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of lercanidipine hydrochloride via coupling reaction of dimethyl(nitrophenyl)pyridinedicarboxylic acid monomethyl ester with [(diphenylpropyl)methylamino](methyl)propanol)
IT 538-75-0, Dicyclohexylcarbodiimide 2592-95-2, 1-Hydroxybenzotriazole 2942-58-7, Diethyl cyanophosphonate
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of lercanidipine hydrochloride via coupling reaction of dimethyl(nitrophenyl)pyridinedicarboxylic acid monomethyl ester with [(diphenylpropyl)methylamino](methyl)propanol)
IT 132866-11-6P, Lercanidipine hydrochloride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of lercanidipine hydrochloride via coupling reaction under mild conditions using convergent synthesis strategy (large-scale synthesis))

L1 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:837814 CAPLUS
DOCUMENT NUMBER: 145:489122
TITLE: Large-scale synthesis of lercanidipine hydrochloride via process under mild condition in presence of coupling reagent
INVENTOR(S): Choi, Jang Sik; Park, Chang Kwon; Suh, Jung Jin
PATENT ASSIGNEE(S): Kun Il Pharm. Co., Ltd., S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2005032781	A	20050408	KR 2003-68738	20031002

PRIORITY APPLN. INFO.: KR 2003-68738 20031002
AB A process for preparing lercanidipine hydrochloride is provided which improves the product yield by performing the process under mild condition in the presence of a coupling reagent, simplifies the process and allows easy removal of a byproduct using water. This process permits the simple and large-scale synthesis of lercanidipine hydrochloride. The process for preparing lercanidipine hydrochloride comprises the reaction of 2,6-dimethyl-5-methoxycarbonyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylic acid with 2,N-dimethyl-N-(3,3-diphenylpropyl)-1-amino-2-propanol in the presence of 2-chloro-1,3-dimethylimidazolium chloride (coupling reagent) and base in solvent at 10-60°. The solvent is selected from dichloromethane, 1,2-dichloroethane and chloroform and the base is pyridine, trimethylamine and triethylamine.
TI Large-scale synthesis of lercanidipine hydrochloride via process under mild condition in presence of coupling reagent
AB A process for preparing lercanidipine hydrochloride is provided which improves the product yield by performing the process under mild condition in the presence of a coupling reagent, simplifies the process and allows easy removal of a byproduct using water. This process permits the simple and large-scale synthesis of lercanidipine hydrochloride. The process for preparing lercanidipine hydrochloride comprises the reaction of 2,6-dimethyl-5-methoxycarbonyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylic acid

with 2,N-dimethyl-N-(3,3-diphenylpropyl)-1-amino-2-propanol in the presence of 2-chloro-1,3-dimethylimidazolium chloride (coupling reagent) and base in solvent at 10-60°. The solvent is selected from dichloromethane, 1,2-dichloroethane and chloroform and the base is pyridine, trimethylamine and triethylamine.

ST lercanidipine hydrochloride prepn imidazolium coupling agent

IT Coupling reaction
(large-scale synthesis of lercanidipine hydrochloride via process under mild condition in presence of dimethyl(chloro)imidazolium chloride as coupling reagent)

IT 132866-11-6P, Lercanidipine hydrochloride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(large-scale synthesis of lercanidipine hydrochloride via process under mild condition in presence of coupling reagent)

IT 74936-72-4, 2,6-Dimethyl-5-methoxycarbonyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylic acid 100442-33-9, 1-[(3,3-Diphenylpropyl)methylamino]-2-methyl-2-propanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(large-scale synthesis of lercanidipine hydrochloride via process under mild condition in presence of coupling reagent)

IT 67-66-3, Chloroform, uses 75-09-2, Dichloromethane, uses 107-06-2, 1,2-Dichloroethane, uses
RL: NUU (Other use, unclassified); USES (Uses)
(large-scale synthesis of lercanidipine hydrochloride via process under mild condition in presence of dimethyl(chloro)imidazolium chloride as coupling reagent)

IT 75-50-3, Trimethylamine, reactions 110-86-1, Pyridine, reactions 121-44-8, Triethylamine, reactions 125376-11-6, 2-Chloro-1,3-dimethylimidazolium chloride
RL: RGT (Reagent); RACT (Reactant or reagent)
(large-scale synthesis of lercanidipine hydrochloride via process under mild condition in presence of dimethyl(chloro)imidazolium chloride as coupling reagent)

L1 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:740305 CAPLUS
DOCUMENT NUMBER: 145:152778
TITLE: Lercanidipine pH-dependent pulsatile release compositions
INVENTOR(S): Abramowitz, Wattanaporn; Kapil, Ram P.; Riccobene, Todd A.; Dedhiya, Mahendra G.; Rastogi, Suneel K.; Chhettry, Anil
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2006165788	A1	20060727	US 2005-223491		20050909
PRIORITY APPLN. INFO.:			US 2004-609222P	P	20040909

AB A modified release composition containing the low solubility and permeability drug, lercanidipine may be prepared that provides for therapeutically effective plasma concns. of lercanidipine for 24 h. The modified release composition of the present invention release pulses of lercanidipine based on the pH of the use environment. An effective quantity of dissolved lercanidipine is released throughout the GI tract. Thus, an immediate-release core

contained lercanidipine-HCl 12.26, Polysorbate-80 0.92, sugar spheres 81.80, Opadry Clear 3.06 (binder), and Opadry Clear (film coating) 1.96%.

IT 100427-26-7, Lercanidipine 132866-11-6, Lercanidipine hydrochloride 185197-71-1, (S)-Lercanidipine
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lercanidipine pH-dependent pulsatile release compns.)

L1 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:740107 CAPLUS
DOCUMENT NUMBER: 145:174347
TITLE: Lercanidipine modified release compositions
INVENTOR(S): Abramowitz, Wattanaporn; Kapil, Ram P.; Riccobene, Todd A.; Dedhiya, Mahendra G.; Yang, Yan; Chhettry, Anil
PATENT ASSIGNEE(S): Forest Laboratories, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2006165789	A1	20060727	US 2005-223493		20050909
PRIORITY APPLN. INFO.:			US 2004-609224P	P	20040909

AB Pursuant to the present invention, it has been found that a modified release composition containing the low permeability and poor solubility drug, lercanidipine, may be prepared which provides for therapeutically effective plasma concns. of lercanidipine for a period of about 20 to about 25 h. The modified release composition of the present invention provides modified release of lercanidipine independent of pH and therefore provides release of lercanidipine even upon exposure to the low pH use environments, such as gastric fluid.

IT 100427-26-7, Lercanidipine 132866-11-6, Lercanidipine hydrochloride
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lercanidipine modified-release compns.)

L1 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:604657 CAPLUS
DOCUMENT NUMBER: 145:89947
TITLE: Lercanidipine immediate release compositions
INVENTOR(S): Dedhiya, Mahendra G.; Rastogi, Suneel K.; Chhettry, Anil
PATENT ASSIGNEE(S): Forest Laboratories, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2006134212	A1	20060622	US 2005-218820		20050902
PRIORITY APPLN. INFO.:			US 2004-606592P	P	20040902

AB The present invention provides an immediate release composition for the low solubility drug, lercanidipine. The immediate release composition of the present

invention comprises a core; a first layer, comprising lercanidipine, a surfactant and a binder, and optionally, a second layer comprising a film coating. Thus, a lercanidipine immediate release bead composition contained Lercanidipine HCl 12.26, Polysorbate 80 0.92, sugar spheres 81.80, Opadry Clear (binder portion) 3.06, and Opadry Clear (film coating portion) 1.96%, resp.

IT 100427-26-7, Lercanidipine 132866-11-6, Lercanidipine hydrochloride 877372-46-8 877372-47-9
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lercanidipine immediate release solid oral compns. comprising inner core, surfactant, binder and optionally film coating)

L1 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:544502 CAPLUS
DOCUMENT NUMBER: 145:45953
TITLE: Intermediates for the preparation of lercanidipine and preparation of lercanidipine from said intermediates
INVENTOR(S): Tomer, Zvulun
PATENT ASSIGNEE(S): Motivan Ltd., Israel
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006059332	A1	20060608	WO 2005-IL1290	20051201

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: IL 2004-165525 A 20041202
OTHER SOURCE(S): CASREACT 145:45953

AB Claimed are intermediates for the preparation of lercanidipine such as 1-chloro-2-methyl-2-Pr Me 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-1-pyridine-3,5-dicarboxylate (I), etc. Thus, reaction of 2,6-dimethyl-5-methoxycarbonyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylic acid with thionyl chloride, followed by reaction with 1-chloro-2-methyl-2-propanol, gave I in 58% yield. Lercanidipine HCl salt was then prepared from I and N-methyl-3,3-diphenylpropylamine. Lercanidipine is a known antihypertensive.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 100427-26-7P, Lercanidipine 132866-11-6P, Lercanidipine hydrochloride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lercanidipine via reaction of 1-halo-2-methyl-2-Pr Me 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-1-pyridine-3,5-dicarboxylate with N-methyl-3,3-diphenylpropylamine)

L1 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:194018 CAPLUS
DOCUMENT NUMBER: 144:260839
TITLE: Preparation of lercanidipine salts
INVENTOR(S): Leonardi, Amadeo; Motta, Gianni; Von Raumer, Markus
PATENT ASSIGNEE(S): Recordati Ireland Limited, Ire.; Recordati Industria Chimica E Farmaceutica S.p.A.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006021397	A1	20060302	WO 2005-EP9043	20050822
WO 2006021397	C1	20060427		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006047125	A1	20060302	US 2005-211769	20050824
PRIORITY APPLN. INFO.:			US 2004-604149P	P 20040824

AB The invention relates to new addition salts comprising lercanidipine and an acid counterion selected from the group consisting of: (i) inorg. acids, (ii) sulfonic acids, (iii) monocarboxylic acids, (iv) dicarboxylic acids, (v) tricarboxylic acids, and (vi) aromatic sulfonimides, with the proviso that said acid counterion is not hydrochloric acid. In particular, both amorphous and crystalline salts of lercanidipine with benzenesulfonic and naphthalene-1,5-disulfonic acids are disclosed, as are amorphous salts of lercanidipine with several other acid counterions. Thus, lercanidipine besylate was prepared and characterized by Raman spectroscopy.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT 100427-26-7DP, Lercanidipine, salts 132866-11-6P, Lercanidipine hydrochloride 877372-41-3P 877372-42-4P 877372-43-5P 877372-44-6P 877372-45-7P 877372-46-8P 877372-47-9P 877372-48-0P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lercanidipine salts)

L1 ANSWER 11 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:46012 CAPLUS
DOCUMENT NUMBER: 145:438491
TITLE: Synthesis of lercanidipine hydrochloride
AUTHOR(S): Liao, Guo-ping; Gao, Rui-chang; Zhang, Guang-ming; Zhang, Jin-feng
CORPORATE SOURCE: Department of Chemical Engineering, Tianjin University, Tianjin, 300072, Peop. Rep. China
SOURCE: Jingxi Huagong (2005), 22(12), 950-951, 954
CODEN: JIHUFJ; ISSN: 1003-5214
PUBLISHER: Jingxi Huagong Bianjibu
DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Alkylation of benzene with cinnamic acid (I) via Fridel-Crafts reaction gave 3,3-diphenyl-propanoic acid (II), which was subsequently converted into the corresponding acid chloride (III) and further converted into N-methyl-3,3-diphenylpropanamide (IV) by reaction with methylamine in methanol. IV was efficiently reduced with the KBH4/ZnCl2 system to give N-methyl-3,3-diphenylpropanamine (V). 2-Methylallyl chloride was hydrated with 80% sulfuric acid to get 1-chloro-2-methyl-2-propanol (VI). Then V reacted with VI to get the key intermediate 2, N-dimethyl-N-(3,3-diphenylpropyl)-1-amino-2-propanol (VII). Finally, VII and 2, 6-dimethyl-4-(3-nitrophenyl)-5-methoxycarboxyl-1,4-dihydropyridine-3-carboxylic acid (DHPCOOH) were connected to form the target product lercanidipine hydrochloride (VIII). Total yield of the seven steps was 23.2%, and structures of the product VIII and key intermediates were verified by ESI - MS and 1HNMR.

TI Synthesis of lercanidipine hydrochloride

AB Alkylation of benzene with cinnamic acid (I) via Fridel-Crafts reaction gave 3,3-diphenyl-propanoic acid (II), which was subsequently converted into the corresponding acid chloride (III) and further converted into N-methyl-3,3-diphenylpropanamide (IV) by reaction with methylamine in methanol. IV was efficiently reduced with the KBH4/ZnCl2 system to give N-methyl-3,3-diphenylpropanamine (V). 2-Methylallyl chloride was hydrated with 80% sulfuric acid to get 1-chloro-2-methyl-2-propanol (VI). Then V reacted with VI to get the key intermediate 2, N-dimethyl-N-(3,3-diphenylpropyl)-1-amino-2-propanol (VII). Finally, VII and 2, 6-dimethyl-4-(3-nitrophenyl)-5-methoxycarboxyl-1,4-dihydropyridine-3-carboxylic acid (DHPCOOH) were connected to form the target product lercanidipine hydrochloride (VIII). Total yield of the seven steps was 23.2%, and structures of the product VIII and key intermediates were verified by ESI - MS and 1HNMR.

ST lercanidipine hydrochloride prepn antihypertensive

IT Alkylation
Antihypertensives
(synthesis of lercanidipine hydrochloride as antihypertensive)

IT 71-43-2, Benzene, reactions 74-89-5, Methylamine, reactions 621-82-9, Cinnamic acid, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of lercanidipine hydrochloride as antihypertensive)

IT 558-42-9P, 1-Chloro-2-methyl-2-propanol 563-47-3P, 2-Methylallyl chloride 606-83-7P, 3,3-Diphenyl-propanoic acid 28075-29-8P 100442-33-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of lercanidipine hydrochloride as antihypertensive)

IT 132866-11-6P, Lercanidipine hydrochloride
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of lercanidipine hydrochloride as antihypertensive)

L1 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:523283 CAPLUS
DOCUMENT NUMBER: 143:65411
TITLE: Pharmaceutical compositions comprising lercanidipine
INVENTOR(S): Holm, Per; Norling, Tomas
PATENT ASSIGNEE(S): Lifecycle Pharma A/S, Den.
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053689	A2	20050616	WO 2004-DK836	20041201
WO 2005053689	A3	20060427		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004294674	A1	20050616	AU 2004-294674	20041201
CA 2547657	AA	20050616	CA 2004-2547657	20041201
EP 1694305	A2	20060830	EP 2004-801160	20041201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
NO 2006003036	A	20060901	NO 2006-3036	20060629

PRIORITY APPLN. INFO.:			
DK 2003-1778	A	20031201
DK 2004-249	A	20040218
US 2004-553787P	P	20040316
US 2004-553787	A	20040316
WO 2004-DK836	W	20041201

AB A controlled release pharmaceutical composition comprising lercanidipine dissolved or dispersed in a solid vehicle at ambient temperature, thus forming a solid dispersion, achieves delayed release of lercanidipine over an extended period of time, reduced food effect and increased bioavailability compared to com. available lercanidipine containing products. Thus, hard gelatin capsules with intragranular hydrocolloid contained lercanidipine HCl 3.811%, Metolose HS 90 100 cP 20.86%, lactose 200 mesh 29.39%, PEG 6000 32.15%, and Poloxamer 188 13.78%.

IT 100427-26-7, Lercanidipine 132866-11-6, Lercanidipine hydrochloride
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lercanidipine oral controlled-release compns. with increased bioavailability)

L1 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:133156 CAPLUS
DOCUMENT NUMBER: 143:83666
TITLE: Determination of lercanidipine hydrochloride and its impurities in tablets
AUTHOR(S): Mihaljica, S.; Radulovic, D.; Trbojevic, J.
CORPORATE SOURCE: Institute of Pharmacy of Serbia, Belgrade, 11152, Yugoslavia
SOURCE: Chromatographia (2005), 61(1/2), 25-29
CODEN: CHRGB7; ISSN: 0009-5893
PUBLISHER: Vieweg Verlag/GWV Fachverlage GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The reversed-phase high-performance liquid chromatog. (RP-HPLC) method was developed for determination of lercanidipine hydrochloride and its synthetic impurities, degradation and oxidative products in Carmen tablets. The best separation was performed on Zorbax SB C18 column, 250

+ 4.6 mm, particle size 5 μm. Acetonitrile-water-triethylamine 55:44.8:0.2 (volume/volume/v) was used as a mobile phase with flow rate 1 mL min-1. PH was adjusted to 3.0 with orthophosphoric acid. UV detection was performed at 240 nm. Duration of chromatog. run was about 12 min for six examined compds. The chromatog. conditions for the determination of lercanidipine hydrochloride and its related substances were the same, but the concentration of lercanidipine hydrochloride was 0.03 mg mL-1 for assay and 0.3 mg mL-1 for related substances. The validation of the method performance characteristics (figures of merits, quality of parameters) was established to be adequate for the intended use. The evaluation of number of parameters, such as selectivity, linearity, accuracy, specificity, precision (repeatability and reproducibility), sensitivity, and detection and determination limits is entailed.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Determination of lercanidipine hydrochloride and its impurities in tablets

AB The reversed-phase high-performance liquid chromatog. (RP-HPLC) method was developed for determination of lercanidipine hydrochloride and its synthetic impurities, degradation and oxidative products in Carmen tablets. The best separation was performed on Zorbax SB C18 column, 250 + 4.6 mm, particle size 5 μm. Acetonitrile-water-triethylamine 55:44.8:0.2 (volume/volume/v) was used as a mobile phase with flow rate 1 mL min-1. PH was adjusted to 3.0 with orthophosphoric acid. UV detection was performed at 240 nm. Duration of chromatog. run was about 12 min for six examined compds. The chromatog. conditions for the determination of lercanidipine hydrochloride and its related substances were the same, but the concentration of lercanidipine hydrochloride was 0.03 mg mL-1 for assay and 0.3 mg mL-1 for related substances. The validation of the method performance characteristics (figures of merits, quality of parameters) was established to be adequate for the intended use. The evaluation of number of parameters, such as selectivity, linearity, accuracy, specificity, precision (repeatability and reproducibility), sensitivity, and detection and determination limits is entailed.

IT Antihypertensives
Impurities
Reversed phase HPLC
(determination of lercanidipine hydrochloride and its impurities in tablets)

IT Drug delivery systems
(tablets; determination of lercanidipine hydrochloride and its impurities in tablets)

IT 39562-70-4 74936-72-4 786625-22-7 855473-53-9 855473-54-0
RL: ANT (Analyte); ANST (Analytical study)
(determination of lercanidipine hydrochloride and its impurities in tablets)

IT 132866-11-6, Lercanidipine hydrochloride
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(determination of lercanidipine hydrochloride and its impurities in tablets)

L1 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:740161 CAPLUS
DOCUMENT NUMBER: 141:254567
TITLE: Combination therapy for hypertension using lercanidipine and an angiotensin II receptor blocker
INVENTOR(S): Sartani, Abraham; Leonardi, Amedeo; Sironi, Giorgio
PATENT ASSIGNEE(S): Recordati Ireland Limited, Ire.; Recordati Industria

Chimica e Farmaceutica S.p.A.
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004075892	A2	20040910	WO 2004-EP2000		20040227
WO 2004075892	A3	20040930			
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004198789	A1	20041007	US 2004-791148		20040301

PRIORITY APPLN. INFO.: US 2003-450782P P 20030228
US 2003-450864P P 20030228
US 2003-478285P P 20030613

AB Lercanidipine is used in the preparation of a medicament for the treatment of hypertension in combination with the prior, concurrent or post-administration of an angiotensin II receptor blocker (ARB) selected from olmesartan, irbesartan, valsartan, telmisartan, losartan and eprosartan, and optionally in further combination with the prior, concurrent or post-administration of a diuretic such as hydrochlorothiazide. Compns. containing lercanidipine and the ARB (or lercanidipine, the ARB and a diuretic) are claimed.

IT 58-93-5, Hydrochlorothiazide 100427-26-7, Lercanidipine 114798-26-4, Losartan 132866-11-6, Lercanidipine hydrochloride 133040-01-4, Eprosartan 137862-53-4, Valsartan 138402-11-6, Irbesartan 144689-24-7, Olmesartan 144701-48-4, Telmisartan 754213-75-7 754213-76-8 754213-77-9 754213-78-0 754213-79-1 754213-80-4 754213-81-5 754213-82-6 754213-83-7 754213-84-8 754213-85-9 754213-86-0 754213-87-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lercanidipine combination with angiotensin II receptor blocker and optional diuretic for treatment of hypertension)

L1 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:648315 CAPLUS
DOCUMENT NUMBER: 141:179622

TITLE: Controlled release pharmaceutical compositions containing polymers

INVENTOR(S): Kannan, Muthaiyyan Esakki; Krishnan, Anandi; Sapre, Beena Amol; Shah, Chitra; Patil, Atul
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004066910	A2	20040812	WO 2004-IB274	20040126
WO 2004066910	C1	20041007		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004185097	A1	20040923	US 2004-762180	20040121
CA 2493899	AA	20040812	CA 2004-2493899	20040126
EP 1599190	A2	20051130	EP 2004-705137	20040126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			IN 2003-MU132	A 20030131
			US 2003-517589P	P 20031105
			IN 2003-MU130	A 20030131
			WO 2004-IB274	W 20040126

AB A solid controlled release pharmaceutical composition suitable comprises a drug, a primary release-modifying agent, a secondary release-modifying agent and an auxiliary release-modifying agent, which are present in amts. that synergistically extend the release of the active ingredient. Thus, tablets contained nicotinic acid 500.00, PEG (mol. weight 4,000,000) 170.0, retrograde starch 40.00, lactose monohydrate 30.00, talc 5.00, and Mg stearate 5.00 mg, and water qs.

IT 40034-42-2, Rosoxacin 42835-25-6, Flumequine 50370-12-2, Cefadroxil 50972-17-3, Bacampicillin 51022-70-9, Salbutamol sulfate 51023-56-4, Ormeloxifene hydrochloride 51481-61-9, Cimetidine 51627-14-6, Cefatrizine 51762-05-1, Cefroxadine 51940-44-4, Pipemidic Acid 52152-93-9, Cefsulodin Sodium 53152-21-9, Buprenorphine hydrochloride 53994-73-3, Cefaclor 54965-24-1, Tamoxifen citrate 55268-75-2, Cefuroxime 55881-07-7, Miocamycin 56187-47-4, Cefazedone 56238-63-2, Cefuroxime sodium 56392-17-7, Metoprolol tartrate 56796-20-4, Cefmetazole 57432-61-8, Methylergometrine maleate 57808-66-9, Domperidone 58665-96-6, Cefazaflur 59729-33-8, Citalopram 60925-61-3, Ceforanide 61270-58-4, Cefonicid 61622-34-2, Cefotiam 62571-86-2, Captopril 62893-19-0, Cefoperazone 63358-49-6, Aspoxicillin 63469-19-2, Apalcillin 63527-52-6, Cefotaxime 64024-15-3, Pentazocine hydrochloride 64044-51-5 64461-82-1, Tizanidine hydrochloride 64544-07-6, Cefuroxime Axetil 65085-01-0, Cefmenoxime 65243-33-6, Cefetamet Pivoxil 65277-42-1, Ketoconazole 66357-59-3, Ranitidine hydrochloride 68401-81-0, Ceftizoxime 68844-77-9, Astemizole 69351-57-1, Dexamethasone hydrochloride 69712-56-7, Cefotetan 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 70797-11-4, Cefpiramide 72558-82-8, Ceftazidime 73384-59-5, Ceftriaxone 73590-58-6, Omeprazole 73963-72-1, Cilostazol 74011-58-8, Enoxacin 74014-51-0, Rokitamycin 74978-16-8, Magaldrate 76095-16-4, Enalapril maleate 76470-66-1, Loracarbef 76610-84-9, Cefbuperazone 77360-52-2, Ceftiolene 78110-38-0, Aztreonam 79350-37-1, Cefixime 79660-72-3, Fleroxacin 79794-75-5, Loratadine 79902-63-9, Simvastatin 80210-62-4, Cefpodoxime 80214-83-1, Roxithromycin 81103-11-9, Clarithromycin 82219-78-1, Cefuzonam 82419-36-1, Ofloxacin 82547-81-7, Cefteram Pivoxil 82664-20-8, Flurithromycin 83905-01-5, Azithromycin 84305-41-9, Cefminox 84625-61-6, Itraconazole 84880-03-5, Cefpimizole 84957-29-9, Cefpirome 84957-30-2, Cefquinome 85721-33-1, Ciprofloxacin 86329-79-5, Cefodizime Sodium 86386-73-4, Fluconazole 86393-37-5, Amifloxacin 87239-81-4, Cefpodoxime Proxetil 88040-23-7, Cefepime 91832-40-5,

Cefdinir 92665-29-7, Cefprozil 93106-60-6, Enrofloxacin 93107-08-5, Ciprofloxacin hydrochloride 93479-97-1, Glimepiride 97240-79-4, Topiramate 97519-39-6, Ceftibuten 98079-51-7, Lomefloxacin 98418-47-4, Metoprolol succinate 99294-93-6, Zolpidem tartrate 100490-36-6, Tosufloxacin 100643-71-8, Desloratadine 100986-85-4, Levofloxacin 101363-10-4, Rufloxacin 102767-28-2, Levetiracetam 105816-04-4, Nateglinide 107133-36-8, Perindopril erbumine 108319-06-8, Temafloxacin 110871-86-8, Sparfloxacin 112811-59-3, Gatifloxacin 112885-41-3, Mosapride 113981-44-5 117211-03-7, Cefetecol 119141-88-7, Esomeprazole 119914-60-2, Grepafloxacin 130018-87-0 132866-11-6, Lercanidipine hydrochloride 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 147059-72-1, Trovafloxacin 151096-09-2, Moxifloxacin 165800-03-3, Linezolid 175463-14-6, Gemifloxacin 181695-72-7, Valdecoxib 287714-41-4, Rosuvastatin 733804-86-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceutical compns. containing polymers)

L1 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:354791 CAPLUS
DOCUMENT NUMBER: 140:344949
TITLE: Lisinopril/lercanidipine combination for the treatment of hypertension
INVENTOR(S): Sartani, Abraham; Leonardi, Amedeo; Sironi, Giorgio
PATENT ASSIGNEE(S): Recordati Ireland Limited, Ire.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004035051	A1	20040429	WO 2003-EP11389		20031015
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003274004	A1	20040504	AU 2003-274004		20031015
EP 1553941	A1	20050720	EP 2003-757976		20031015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2006504800	T2	20060209	JP 2005-501292		20031015
PRIORITY APPLN. INFO.:			US 2002-419790P	P	20021016
			IT 2002-MI2594	A	20021206
			WO 2003-EP11389	W	20031015

AB Pharmaceutical compns. for the treatment of hypertension, comprising a lisinopril/lercanidipine combination, suitable to decrease blood pressure and maintaining min. side effects, are described. A tablet contained lercanidipine hydrochloride 10, lisinopril (as dihydrate) 10, lactose 102, microcryst. cellulose 40, sodium bicarbonate 8, sodium starch glycolate 20, povidone K30 8, and magnesium stearate 2 mg. Coating of the tablet comprised hypromellose 1.91, talc 0.15, titanium dioxide 0.60, Macrogol-6000 0.30, and ferric oxide 0.04 mg. Combination treatment with lisinopril and lercanidipine lead to significantly greater decreases in both systolic blood pressure and

diastolic blood pressure in rats as compared to vehicle or lisinopril or lercanidipine alone.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Pharmaceutical compns. for the treatment of hypertension, comprising a lisinopril/lercanidipine combination, suitable to decrease blood pressure and maintaining min. side effects, are described. A tablet contained lercanidipine hydrochloride 10, lisinopril (as dihydrate) 10, lactose 102, microcryst. cellulose 40, sodium bicarbonate 8, sodium starch glycolate 20, povidone K30 8, and magnesium stearate 2 mg. Coating of the tablet comprised hypromellose 1.91, talc 0.15, titanium dioxide 0.60, Macrogol-6000 0.30, and ferric oxide 0.04 mg. Combination treatment with lisinopril and lercanidipine lead to significantly greater decreases in both systolic blood pressure and diastolic blood pressure in rats as compared to vehicle or lisinopril or lercanidipine alone.

IT 76547-98-3, Lisinopril 83915-83-7, Lisinopril dihydrate 100427-26-7, Lercanidipine 132866-11-6, Lercanidipine hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lisinopril/lercanidipine combination for treatment of hypertension)

L1 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:757021 CAPLUS
DOCUMENT NUMBER: 139:255360
TITLE: Combination therapy of enalapril and lercanidipine for hypertension
INVENTOR(S): Leonardi, Amedeo; Sartani, Abraham; Sironi, Giorgio
PATENT ASSIGNEE(S): Italy
SOURCE: U.S. Pat. Appl. Publ., 23 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003180355	A1	20030925	US 2002-274430		20021016
PRIORITY APPLN. INFO.:			IT 2001-MI2136	A	20011016
			US 2001-344601P	P	20011023

AB Disclosed are compns. and methods for treating hypertension comprising enalapril and lercanidipine in amts. effective in combination to reduce blood pressure to a patent in need of treatment. Addition of 20 mg lercanidipine to existing enalapril therapy decreased sitting diastolic blood pressure values greater than would be suggested when enalapril and lercanidipine were administered as monotherapies.

IT 76095-16-4, Enalapril maleate 132866-11-6, Lercanidipine hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enalapril and lercanidipine combination for treating hypertension)

L1 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:529125 CAPLUS
DOCUMENT NUMBER: 139:173529
TITLE: Improved tolerability of the dihydropyridine calcium-channel antagonist lercanidipine: the lercanidipine challenge trial
AUTHOR(S): Borghi, Claudio; Prandin, Maria Grazia; Dormi, Ada; Ambrosioni, Ettore; Battistini, G.; Bellei, M.; Fantini, E.; Panuccio, D.; Querze, M.; Ippolito, F.; Rastelli, G.; Tartagni, F.; Orlandi, P.
CORPORATE SOURCE: Department of Internal Medicine, Study Group of the

Regional Unit of the Italian Society of Hypertension, University of Bologna, Bologna, Italy
SOURCE: Blood Pressure, Supplement (2003), (1), 14-21
CODEN: BPSUEY; ISSN: 0803-8023
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objective of this 8-wk open-label study was to compare the tolerability of lercanidipine, a dihydropyridine calcium-channel antagonist (CA), with that of other CAs in the treatment of hypertension. Subjects already taking amlodipine, felodipine, nifedipine gastrointestinal therapeutic system (GITS), or nitrendipine and experiencing CA-specific adverse effects (AEs) were switched to lercanidipine for 4 wk and then rechallenged with their initial treatment for 4 wk. Results showed that at comparable levels of BP, lercanidipine was associated with a significantly lower incidence of ankle edema, flushing, rash, headache and dizziness compared with other CAs ($p < 0.001$). After 4 wk of lercanidipine, mean systolic blood pressure (SBP)/diastolic blood pressure (DBP) was 142.1/86.7 mmHg. After rechallenge with other CAs for 4 wk, mean SBP/DBP was 141.1/86.7 mmHg. In this open-label study, lercanidipine compared with other CA seems to provide a significant improvement in tolerability with comparable antihypertensive effect.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 132866-11-6, Lercanidipine hydrochloride
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy of lercanidipine in treatment of hypertension)

L1 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:133241 CAPLUS
DOCUMENT NUMBER: 138:175893
TITLE: Solvates and crystalline forms of lercanidipine hydrochloride
INVENTOR(S): Leonardi, Amedeo; De Iasi, Gianluca; Bonifacio, Fausto
PATENT ASSIGNEE(S): Recordati Ireland Limited, Ire.
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014085	A1	20030220	WO 2002-EP8700	20020805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1423367	A1	20040602	EP 2002-767318	20020805
EP 1423367	B1	20050427		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011738	A	20040928	BR 2002-11738	20020805
HU 200401161	A2	20040928	HU 2004-1161	20020805
CN 1538958	A	20041020	CN 2002-815511	20020805

JP 2005502648	T2	20050127	JP 2003-519035		20020805
AT 294162	E	20050515	AT 2002-767318		20020805
CA 2399459	AA	20030206	CA 2002-2399459		20020806
CA 2399583	AA	20030206	CA 2002-2399583		20020806
US 2003069285	A1	20030410	US 2002-214385		20020806
US 2003083355	A1	20030501	US 2002-214386		20020806
US 6852737	B2	20050208			
NO 2004000479	A	20040203	NO 2004-479		20040203
US 2004204459	A1	20041014	US 2004-782376		20040218
US 2005192323	A1	20050901	US 2005-48646		20050131
US 2005239847	A1	20051027	US 2005-48647		20050131
PRIORITY APPLN. INFO.:			IT 2001-MI1727	A	20010806
			IT 2001-MI1726	A	20010806
			US 2002-367789P	P	20020326
			CA 2002-2380202	A	20020403
			WO 2002-EP8700	W	20020805
			US 2002-214386	A3	20020806

AB The invention describes new solvates of lercanidipine-HCl with organic solvents, new crystalline forms III and IV obtained from said solvates by removing solvation solvents, and pharmaceutical compns. containing as active agent at least one of the crystalline forms III and IV.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Solvates and crystalline forms of lercanidipine hydrochloride

ST lercanidipine hydrochloride solvate org cryst form

IT Crystal morphology
Crystallization
Drug delivery systems
Solvates
(solvates and crystalline forms of lercanidipine hydrochloride)

IT 75-09-2, Methylene chloride, reactions
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(solvates and crystalline forms of lercanidipine hydrochloride)

IT 132866-11-6P, Lercanidipine hydrochloride
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(solvates and crystalline forms of lercanidipine hydrochloride)

IT 497859-62-8P, Lercanidipine hydrochloride
497859-63-9P, Lercanidipine hydrochloride
497859-64-0P, Lercanidipine hydrochloride
497859-65-1P, Lercanidipine hydrochloride
497859-66-2P, Lercanidipine hydrochloride
497859-67-3P, Lercanidipine hydrochloride
497859-68-4P, Lercanidipine hydrochloride
497859-69-5P, Lercanidipine hydrochloride
497859-70-8P, Lercanidipine hydrochloride
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(solvates and crystalline forms of lercanidipine hydrochloride)

L1 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:133240 CAPLUS
DOCUMENT NUMBER: 138:193269
TITLE: Novel crystalline polymorphic forms of lercanidipine hydrochloride and process for their preparation

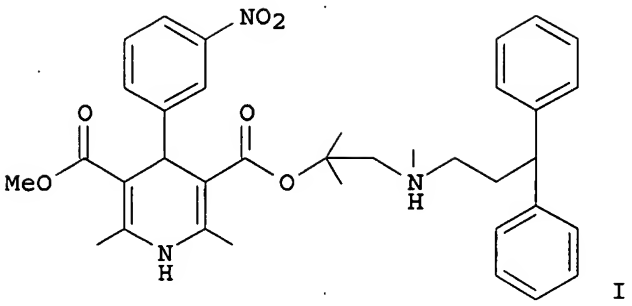
10/782,376

INVENTOR(S): Bonifacio, Fausto; Campana, Francesco; De Iasi, Gianluca; Leonardi, Amedeo
PATENT ASSIGNEE(S): Recordati Ireland Limited, Ire.
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014084	A1	20030220	WO 2002-EP8699	20020805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2380202	AA	20030206	CA 2002-2380202	20020403
EP 1432683	A1	20040630	EP 2002-762428	20020805
EP 1432683	B1	20051019		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011739	A	20040928	BR 2002-11739	20020805
HU 200401163	A2	20040928	HU 2004-1163	20020805
CN 1538957	A	20041020	CN 2002-815413	20020805
JP 2005504045	T2	20050210	JP 2003-519034	20020805
AT 307114	E	20051115	AT 2002-762428	20020805
IL 153917	A1	20051120	IL 2002-153917	20020805
EP 1600441	A2	20051130	EP 2005-106264	20020805
EP 1600441	A3	20051207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
NZ 531558	A	20051223	NZ 2002-531558	20020805
ES 2212759	T3	20060416	ES 2002-2762428	20020805
CA 2399459	AA	20030206	CA 2002-2399459	20020806
CA 2399583	AA	20030206	CA 2002-2399583	20020806
US 2003069285	A1	20030410	US 2002-214385	20020806
US 2003083355	A1	20030501	US 2002-214386	20020806
US 6852737	B2	20050208		
NO 2004000266	A	20040324	NO 2004-266	20040120
US 2004204459	A1	20041014	US 2004-782376	20040218
ZA 2004001806	A	20050418	ZA 2004-1806	20040304
HK 1067123	A1	20060526	HK 2004-110181	20041223
US 2005192323	A1	20050901	US 2005-48646	20050131
US 2005239847	A1	20051027	US 2005-48647	20050131

PRIORITY APPLN. INFO.:		
IT 2001-MI1726	A	20010806
US 2002-367789P	P	20020326
IT 2001-MI1727	A	20010806
CA 2002-2380202	A	20020403
EP 2002-762428	A3	20020805
WO 2002-EP8699	W	20020805
US 2002-214386	A3	20020806

GI



I

AB The invention describes novel lercanidipine (I) crude forms (A) and (B), novel I-HCl crystalline forms I and II obtained from crude forms, pharmaceutical, antihypertensive compns. containing as active agent at least one of the I-HCl crystalline forms I and II and methods of use. I-HCl was prepared and the crystalline forms obtained by crystallization from various solvents.

The bioavailability of the various forms was also determined

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Novel crystalline polymorphic forms of lercanidipine hydrochloride and process for their preparation

ST lercanidipine hydrochloride crystal form

IT Antihypertensives
Crystal morphology
Drug bioavailability
Human
(crystalline polymorphic forms of lercanidipine hydrochloride)

IT 132866-11-6P, Lercanidipine hydrochloride
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline polymorphic forms of lercanidipine hydrochloride)

IT 64-17-5, Ethanol, processes 67-63-0, Isopropanol, processes 141-78-6, Ethyl acetate, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(crystalline polymorphic forms of lercanidipine hydrochloride)

IT 74936-72-4 100442-33-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(crystalline polymorphic forms of lercanidipine hydrochloride)

IT 88712-56-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(crystalline polymorphic forms of lercanidipine hydrochloride)

L1 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:58603 CAPLUS

DOCUMENT NUMBER: 128:175676

TITLE: Lercanidipine (Rec 15/2375): a novel 1,4-dihydropyridine calcium antagonist for hypertension

AUTHOR(S): Testa, R.; Leonardi, A.; Tajana, A.; Riscassi, E.; Magliocca, R.; Sartani, A.

CORPORATE SOURCE: Pharmaceutical RandD Division, Recordati S.p.A., Milan, 20148, Italy
SOURCE: Cardiovascular Drug Reviews (1997), 15(3), 187-219
CODEN: CDREEA; ISSN: 0897-5957
PUBLISHER: Neva Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 76 refs.
REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT 132866-11-6, Rec 15/2375
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lercanidipine hydrochloride; novel 1,4-dihydropyridine calcium antagonist for hypertension)

L1 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:204232 CAPLUS
DOCUMENT NUMBER: 126:195245
TITLE: Use of 1,4-dihydropyridine derivatives in the prevention and therapy of atherosclerotic degradation of arterial walls
INVENTOR(S): Sartani, Abraham; Leonardi, Amedeo; Testa, Rodolfo
PATENT ASSIGNEE(S): Recordati S.A., Chemical and Pharmaceutical Company, Switz.; Recordati Industria Chimica E Farmaceutica S.P.A.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9703669	A1	19970206	WO 1996-EP2872	19960628
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5767136	A	19980616	US 1996-645964	19960510
US 5912351	A	19990615	US 1996-645963	19960510
CA 2219501	AA	19970206	CA 1996-2219501	19960628
AU 9665164	A1	19970218	AU 1996-65164	19960628
AU 690471	B2	19980423		
EP 839036	A1	19980506	EP 1996-924834	19960628
EP 839036	B1	19990825		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1190345	A	19980812	CN 1996-195439	19960628
HU 9802736	A2	19990329	HU 1998-2736	19960628
JP 11509214.	T2	19990817	JP 1996-506222	19960628
AT 183644	E	19990915	AT 1996-924834	19960628
ES 2138359	T3	20000101	ES 1996-924834	19960628
IL 122302	A1	20000813	IL 1996-122302	19960628
ZA 9605924	A	19970130	ZA 1996-5924	19960712
NO 9800171	A	19980114	NO 1998-171	19980114
PRIORITY APPLN. INFO.:			IT 1995-MI1513 A	19950714
			IT 1995-MI957 A	19950512

WO 1996-EP2872 W 19960628

OTHER SOURCE(S): MARPAT 126:195245

AB 1,4-Dihyropyridines have been found to counter several processes which play a role in the development of atherosclerotic vascular lesions, such as myocytes proliferation and migration, cholesterol metabolism in macrophages and oxidative modification of low d. lipoproteins. They are therefore useful in the manufacture of medicaments for preventing, arresting and reversing atherosclerotic degradation in the arterial walls of humans. The preferred 1,4-dihydropyridines for this purpose are lercanidipine, (S)-lercanidipine and (R)-lercanidipine (preparation given). Lercanidipine and its enantiomers proved able to inhibit, in a concentration-dependent way, up to 90% of the formation of esterified cholesterol induced by acetyl LDL in mouse peritoneal macrophage. The IC50 values for lercanidipine and its enantiomers ranged from 8-15 μM, the (R)-enantiomer being the most active compound

IT 3337-17-5P, 1,4-Dihydropyridine 132866-11-6P, Lercanidipine hydrochloride 184866-29-3P 187731-34-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1,4-dihydropyridine derivs. for prevention and therapy of atherosclerotic degradation of arterial walls)

L1 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:34056 CAPLUS
DOCUMENT NUMBER: 126:59871
TITLE: Preparation of lercanidipine hydrochloride.
INVENTOR(S): Leonardi, Amedeo; Motta, Gianni
PATENT ASSIGNEE(S): Recordati S.A., Chemical and Pharmaceutical Company, Switz.; Recordati Industria Chimica E Farmaceutica S.P.A.
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9635668	A1	19961114	WO 1996-EP2122	19960509
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
IL 118143	A1	20010614	IL 1996-118143	19960503
IN 188486	A1	20021005	IN 1996-CA822	19960506
CA 2217849	AA	19961114	CA 1996-2217849	19960509
AU 9658985	A1	19961129	AU 1996-58985	19960509
AU 694046	B2	19980709		
EP 824517	A1	19980225	EP 1996-916111	19960509
EP 824517	B1	20020724		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1184468	A	19980610	CN 1996-193842	19960509
CN 1101810	B	20030219		
HU 9801913	A2	19981228	HU 1998-1913	19960509
JP 11504932	T2	19990511	JP 1996-533797	19960509
BR 9608374	A	19990824	BR 1996-8374	19960509
EE 3351	B1	20010215	EE 1997-303	19960509

CZ 288634	B6	20010815	CZ 1997-3567		19960509
EG 21755	A	20020227	EG 1996-402		19960509
AT 221050	E	20020815	AT 1996-916111		19960509
PT 824517	T	20021231	PT 1996-916111		19960509
ES 2179942	T3	20030201	ES 1996-916111		19960509
PL 185260	B1	20030430	PL 1996-323236		19960509
SK 283321	B6	20030603	SK 1997-1514		19960509
RO 119616	B1	20050128	RO 1997-2101		19960509
ZA 9603716	A	19961120	ZA 1996-3716		19960510
US 5767136	A	19980616	US 1996-645964		19960510
US 5912351	A	19990615	US 1996-645963		19960510
TW 404940	B	20000911	TW 1996-85105567		19960510
NO 9705176	A	19971111	NO 1997-5176		19971111
NO 309423	B1	20010129			
PRIORITY APPLN. INFO.:			IT 1995-MI957	A	19950512
			IT 1995-MI1513	A	19950714
			WO 1996-EP2122	W	19960509

OTHER SOURCE(S): CASREACT 126:59871

AB Me 1,1,N-trimethyl-N-(3,3-diphenylpropyl)-2-aminoethyl 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate (lercanidipine) hydrochloride (I) was prepared by halogenating 2,6-dimethyl-5-methoxycarbonyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylic acid in an aprotic solvent and adding 2,N-dimethyl-N-(3,3-diphenylpropyl)-1-amino-2-propanol in an aprotic solvent, and isolating the resultant anhydrous I. I can be isolated by industrially applicable crystallization techniques and was obtained in high (78%) yield as its anhydrous hydrochloride, a form which possesses increased heat stability relative to the hemihydrate.

TI Preparation of lercanidipine hydrochloride.

AB Me 1,1,N-trimethyl-N-(3,3-diphenylpropyl)-2-aminoethyl 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate (lercanidipine) hydrochloride (I) was prepared by halogenating 2,6-dimethyl-5-methoxycarbonyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylic acid in an aprotic solvent and adding 2,N-dimethyl-N-(3,3-diphenylpropyl)-1-amino-2-propanol in an aprotic solvent, and isolating the resultant anhydrous I. I can be isolated by industrially applicable crystallization techniques and was obtained in high (78%) yield as its anhydrous hydrochloride, a form which possesses increased heat stability relative to the hemihydrate.

ST lercanidipine hydrochloride anhyd prepn

IT 132866-11-6P, Lercanidipine hydrochloride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of lercanidipine hydrochloride)

IT 74936-72-4, 2,6-Dimethyl-5-methoxycarbonyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylic acid 100442-33-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of lercanidipine hydrochloride)

L1 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1996:260102 CAPLUS
DOCUMENT NUMBER:	124:307070
TITLE:	Hemodynamic effects of lercanidipine in anesthetized open-chest dogs
AUTHOR(S):	Sironi, Giorgio; Montagna, Ernesto; Greto, Luigi; Leonardi, Amedo; Testa, Rodolfo
CORPORATE SOURCE:	Pharmaceutical R&D Div., Recordati S.p.A., Milan, Italy
SOURCE:	Arzneimittel-Forschung (1996), 46(3), 256-61 CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER:	Cantor

DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this study, the hemodynamic effects of lercanidipine (CAS 132866-11-6, Rec 15/2375) in anesthetized open-chest dogs were investigated in comparison with nitrendipine. I.v. administered lercanidipine induced a dose-related, long lasting reduction in systemic and coronary vascular resistances, with concomitant decrease in arterial blood pressure and increase in coronary blood flow. The hypotensive ED25 was 6.1 μg/kg and 4.2 μg/kg (decrease of mean blood pressure and of total peripheral resistances, resp.) and the ED50 on coronary vasodilation, 4.8 μg/kg and 7.8 μg/kg (increase of coronary blood flow and decrease in coronary vascular resistances, resp.). The time-course of the hemodynamic effects was investigated after administration of 5 μg/kg. A slow onset of hemodynamic vasodilation and long-lasting activity were observed, since peak effects on mean blood pressure and coronary blood flow occurred at 20 and 30 min after the administration, resp., and the effects on systemic and coronary resistances were still significant at 30 and 150 min after administration, resp.
IT 132866-11-6, Rec 15/2375
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lercanidipine hydrochloride; hemodynamic effects of lercanidipine in anesthetized open-chest dogs)

L1 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:197932 CAPLUS
DOCUMENT NUMBER: 124:306913
TITLE: Antihypertensive effects of lercanidipine in experimental hypertensive rats and dogs
AUTHOR(S): Sironi, Giorgio; Montagna, Ernesto; Greto, Luigi; Bianchi, Giorgio; Leonardi, Amedeo; Testa, Rodolfo
CORPORATE SOURCE: Research and Development Division, Recordati S.p.A., Milan, Italy
SOURCE: Arzneimittel-Forschung (1996), 46(2), 145-52
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Cantor
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antihypertensive action of lercanidipine (CAS 132866-11-6, Rec 15/2375), a new 1,4-dihydropyridine (1,4-DHP) calcium entry blocker (CEB), was examined in spontaneously hypertensive rats (SHR) and renal hypertensive dogs after acute and repeated administration, in comparison to several reference 1,4-DHPs. In acute expts. in SHR, lercanidipine reduced diastolic blood pressure showing a potency similar to felodipine and 2-3 fold higher than those of nicardipine and nitrendipine, after both i.v. and oral administration. Anal. of the area under the curves of percent reduction of diastolic blood pressure exerted for 3 and 8 h after i.v. and oral administrations, resp., showed that the duration of the antihypertensive effect of lercanidipine was longer than that of the reference dihydropyridines. After repeated administrations to SHR no tachyphylaxis was observed, as indicated by the marked and persistent decrease in systolic blood pressure elicited by lercanidipine, given orally once a day for 21 days. Moreover, starting from the first week of treatment, the daily basal values of systolic blood pressure of the rats treated with lercanidipine were significantly lower than those of the placebo-treated group. In renal hypertensive dogs, after acute oral administration, lercanidipine was as potent as nitrendipine. After repeated administration, the action of lercanidipine was longer lasting than that of nicardipine and no decrease in the antihypertensive effects was observed The in vivo studies show that lercanidipine has a potent and long-lasting antihypertensive profile, suggesting that this compound may be used for once-a-day treatment.
IT 132866-11-6, Lercanidipine hydrochloride

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antihypertensive effects of lercanidipine in exptl. hypertensive rats and dogs)

L1 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:174557 CAPLUS
DOCUMENT NUMBER: 124:250406
TITLE: Pharmacological in vitro studies of the new 1,4-dihydropyridine calcium antagonist lercanidipine
AUTHOR(S): Guarneri, Luciano; Angelico, Patrizia; Ibba, Marina; Poggesi, Elena; Taddei, Carlo; Leonardi, Amedeo; Testa, Rodolfo
CORPORATE SOURCE: Pharmaceutical R&D Division, Recordati S.p.A., Milan, Italy
SOURCE: Arzneimittel-Forschung (1996), 46(1), 15-24
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Cantor
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present studies were undertaken to examine the in vitro calcium antagonistic properties of lercanidipine (CAS 132866-11-6, Rec 15/2375) in vascular and non-vascular tissues, as well as its binding profile and in particular its affinity to the calcium channel binding sites. Lercanidipine proved to be endowed with high affinity for the hydropyridine subunit of the L-type calcium channel, where it was much more potent than on the other receptors tested. The nature of the interaction of lercanidipine with the calcium channel appears competitive, as evidence by a progressive increase in the apparent Kd of the ligand with no change in Bmax. The performed functional in vitro studies in isolated vascular and cardiac tissues demonstrated that lercanidipine has a slower onset and offset of calcium antagonistic activity compared with other calcium antagonists. The time-course of inhibition of vascular smooth muscle contraction showed substantial differences after addition of lercanidipine with regard to the other calcium antagonists tested (nitrendipine and amlodipine). On repeated washing of rat aorta to remove the drugs from the preparation, the effects of nitrendipine disappeared rapidly. After amlodipine incubation, contractility of the tissue was still impaired after 6 h washout with the highest concns. tested, but completely recovered in 1-3 h after washout of the lowest concentration On the contrary, the prepns. incubated with lercanidipine showed a decrease in contractility that reached the maximum 1 to 3 h after the removal of the compound from the bath at all the active concns. tested. The functional calcium antagonistic activity of lercanidipine showed a decrease in contractility that reached the maximum 1 to 3 h after the removal of the compound from the bath at all the active concns. tested. The functional calcium antagonistic activity of lercanidipine showed a decrease in contractility that reached the maximum 1 to 3 h after the removal of the compound from the bath at all the active concns. tested. The functional calcium antagonistic activity of lercanidipine showed a decrease in contractility that reached the maximum 1 to 3 h after the removal of the compound from the bath at all the active concns. tested. The functional calcium antagonistic activity of lercanidipine was also evaluated as relaxing potency against the tonic contractions induced by preincubation of rat aorta, bladder and colon with 80 mmol/l K+. In rat aorta, lercanidipine proved more potent than nitrendipine. Comparing the IC50 values evaluated after 3 h of contact time, lercanidipine resulted more active on the vascular tissue with potency ratios of 177 and 8.5 for aorta vs. bladder and aorta vs. colon, resp. In contrast, nitrendipine showed about the same activity in the three tested tissues, and potency ratios of 2.0 and 0.8 for aorta vs. bladder and aorta vs. colon were calculated In rat aortic strips maintained during the incubation with lercanidipine at

different degrees of depolarization, the functional calcium antagonistic activity markedly increased by raising the tissue depolarization, the functional calcium antagonistic activity markedly increased by raising the tissues depolarization and the potency ratio between the IC50 values evaluated at 5 and 100 mmol/l K+ resulted 138. Nitrendipine provided very similar results, whereas nifedipine activity did not seem to be affected by raising the tissue depolarization. The neg. inotropic effects of lercanidipine on normally and partially depolarized rabbit ventricular strips, as well as in guinea-pig atria, were negligible in comparison to its effects on vasculature. On the whole these characteristics suggest a slow onset of action and long duration of effects also after in vivo administration. In addition, the unique vascular selectivity of lercanidipine implies that the therapeutically desirable vasodilator activity is not or scarcely associated with a decrease in cardiac contractile force.

IT 132866-11-6, Rec 15/2375
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lercanidipine hydrochloride; pharmacol. in vitro studies of the new dihydropyridine calcium antagonist lercanidipine)

L1 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:996589 CAPLUS
DOCUMENT NUMBER: 124:45676
TITLE: Immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods
INVENTOR(S): Mak, Vivien H. W.
PATENT ASSIGNEE(S): De Novo Corp, USA
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9527510	A1	19951019	WO 1995-US4677	19950411
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9523857	A1	19951030	AU 1995-23857	19950411
EP 757558	A1	19970212	EP 1995-917009	19950411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10500669	T2	19980120	JP 1995-526541	19950411
EP 937460	A2	19990825	EP 1999-201333	19950411
EP 937460	A3	20000405		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 5962477	A	19991005	US 1998-97441	19980615
US 6190691	B1	20010220	US 1998-97440	19980615

PRIORITY APPLN. INFO.:

US 1994-225991	A2	19940412
US 1994-271287	A	19940706
US 1995-400234	A	19950303
EP 1995-917009	A3	19950411
WO 1995-US4677	W	19950411
US 1995-463819	B1	19950605

AB Screening methods are provided for evaluating compds. capable of

suppressing cytokine production either in vitro or in vivo. The methods generally involve stimulating the production of a cytokine in a cell, exposing a portion of the cells to a putative cytokine-modulating agent, and determining subsequent levels of cytokine production in the cells. Addnl., the present invention provides certain compds. identified by this method, as well as methods for treating conditions modulated by TNF. The methodol. of the invention may be used for e.g. prevention or reduction of transdermal drug delivery system-induced irritation and treatment of skin or systemic inflammatory conditions. Examples include e.g. inhibition of stimulated cytokine production in human cells by a variety of drugs. Verapamil was effective in preventing the development of skin inflammatory responses in mice.

IT 132866-11-6, Rec 15/2375
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lercanidipine hydrochloride; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

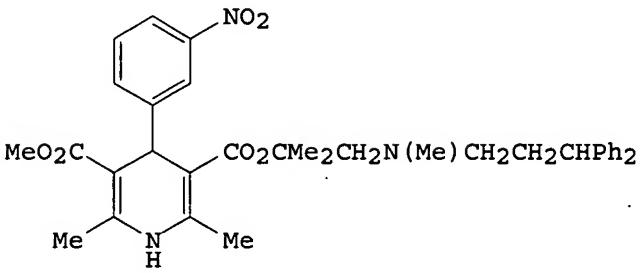
L1 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:400475 CAPLUS
DOCUMENT NUMBER: 111:475
TITLE: Effects of a new calcium antagonist, Rec 15/2375, on cardiac contractility of conscious rabbits
AUTHOR(S): Bianchi, G.; Passoni, A.; Griffini, P. L.
CORPORATE SOURCE: Dep. Pharmacol., Recordati S.p.A., Milan, Italy
SOURCE: Pharmacological Research (1989), 21(2), 193-200
CODEN: PHMREP; ISSN: 1043-6618
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The new Ca2+ antagonist Rec 15/2375, reported to be selective for the vascular tissue, was compared to nifedipine, a nonselective agent that reduces blood pressure and impairs cardiac inotropism as well. Rabbits, chronically catheterized and continuously monitored for systemic blood pressure, heart rate, and the isovolumic contractility index dP/dTmax, were alternatively treated with Rec 15/2375 and nifedipine. Both drugs were given under either autonomically intact (AI) or suppressed (AS) heart function control, induced by cholinergic and β-adrenoceptor blockade. The 2 agents reduced mean arterial blood pressure comparably and dose-dependetly under both exptl. conditions (10-40%), thus causing heart rate to increase reflexly, similarly between drugs in AI rabbits, whereas the AS maneuver totally abolished such a response. Cardiac contractility, on the other hand, displayed opposing behavior between the 2 drugs. Rec 15/2375 caused mild increases, which were similar at all doses (+10, +15%) and insensitive to the AS intervention, whereas nifedipine caused dose-dependent redns. (10-60%) of comparable intensity as mean blood pressure decreases in both protocols. Thus, Rec 15/2375 effectively lowers blood pressure with no impairment, unlike nifedipine, of cardiac inotropism. The possibility that dP/dTmax may be increased as a result of the hemodynamic rearrangement following after-load reduction is discussed.

IT 132866-11-6, Rec 15-2375
RL: BIOL (Biological study)
(lercanidipine hydrochloride; hypertension decrease by, heart inotropy response to)

L1 ANSWER 29 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:602929 CAPLUS
DOCUMENT NUMBER: 105:202929
TITLE: Long lasting anti-hypertensive effects after oral Rec 15/2375, a new non-tachycardic calcium entry blocker, in conscious dogs
AUTHOR(S): Bianchi, Giorgio; Greto, Luigi; Comolatti, Giampiero;

Ceserani, Roberto
CORPORATE SOURCE: Sezione Farmacol., Recordati S.p.A., Milano, 20148, Italy
SOURCE: IRCS Medical Science (1986), 14(8), 817-18
CODEN: IMSCE2; ISSN: 0268-8220
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB In dogs with exptl. (renal) hypertension, Rec 15/2375 (I) [100427-26-7] had a long-lasting antihypertensive activity without any tachycardiac effect. Thus, I appears to be a safe dihydropyridine derivative for the treatment of hypertension.

IT 132866-11-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lercanidipine hydrochloride; antihypertensive activity of, heart rate response in)

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